CLAIMS

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1. A polynucleotide which:

(a) encodes a polypeptide that has the properties of a methylarginase, which polynucleotide is selected from:

(1) the coding sequence of SEQ ID NO: 1, 3, 5, 7, 9 or 11;

(2) a sequence which hybridises selectively to the complement of a sequence defined in (1); and

(3) a sequence that is degenerate as a result of the genetic code with respect to a sequence defined in (1) or (2); or

(b) is a sequence complementary to a polynucleotide defined in (a).

2. A polynucleotide according to claim 1 which is a DNA sequence.

3. A polynucleotide according to claim 1 or 2 which encodes the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10 or 12.

4. A polynucleotide which comprises the coding sequence of SEQ ID NO: 1, 3, 5, 7, 9 or 11 or a fragment thereof.

5. A polypeptide which has methylarginase activity and which comprises the sequence set out in SEQ ID NO: 2, 4, 6, 8, 10 or 12, a sequence substantially homologous thereto or a fragment of either said sequence.

6. A vector incorporating a polynucleotide as defined in any one of claims 1 to 4.

7. A vector according to claim 6, which is an expression vector.

8. A cell harbouring a polynucleotide according to any one of claims 4, a peptide according to claim 5 or vector according to claim 6 or 7.

9. A process for the preparation of a polypeptide which has methylarginase activity, which process comprises cultivating a host cell harbouring an expression vector according to claim 7 under conditions to provide for expression of the said polypeptide, and recovering the expressed polypeptide.

10. An antibody capable of binding a polypeptide encoded by a

polynucleotide according to any of claims 1 to 4 or a polypeptide according to claim 5.

11. A non-human animal which is not capable of expressing or is not capable of expressing an active form of one or more isoforms of methylarginase.

12. A non-human animal according to claim 11 wherein the methylarginase isoform is a dimethylarginine dimethylaminohydroase I (DDAHI).

13. A non-human animal according to claim 11 or 12 wherein the methylarginase isoform is a dimethylarginine dimethylaminohydroase II (DDAHII).

14. A non-human animal according to any one of claims 11 to 13 which is a transgenic animal.

15. A non-human animal according to any one of claims 11 to 14 which is a mouse.

16. A modulator of methylarginase activity and/or expression.

17. A modulator according to claim 16, wherein the methylarginase is a DDAHI.

18. A modulator according to claim 16, wherein the methylarginase is a DDAHII.

19. A modulator according to any one of claims 16 to 18, which is an inhibitor of methylarginase activity and/or expression.

20. A modulator according to any one of claims 16 to 18, which is an activator of methylarginase activity and/or expression.

21. A method for identifying a modulator of methylarginase activity and/or expression, comprising:

(i) contacting a polynucleotide according to any one of claims 1 to 4, a polypeptide according to claim 5, a vector according to claim 7 or a cell according to claim 8 and a test substance under conditions that would permit methylarginase activity in the absence of the test substance; and

(ii) determining thereby whether the said substance modulates the activity and/or expression of methylarginase.

22. A modulator of methylarginase activity and/or expression identified by

the method of claim 21.

23. A modulator according to claim 22, wherein the methylarginase is a DDAHI.

24. A modulator according to claims 22, wherein the methylarginase is a DDAHII.

25. A modulator according to any one of claims 22 to 24, which is an inhibitor of methylarginase activity and/or expression.

26. A modulator according to any one of claims 22 to 24, which is an activator of methylarginase activity and/or expression.

27. A polynucleotide according to any one of claims 1 to 4, a polypeptide according to claim 5, an expression vector according to claim 7 or a modulator according to any one of claims 16 to 20 or 22 to 26 for use in a method of treatment of the human or animal body by therapy.

28. A polynucleotide according to any one of claims 1 to 4, a polypeptide according to claim 5, an expression vector according to claim 7 or a modulator according to claim 20 or 26 for use in a method of treatment of hyperlipidaemia, renal failure, hypertension, restenosis after angioplasty, atherosclerosis, complications of heart failure, schizophrenia, multiple sclerosis or cancer.

29. A modulator according to claim 19 or 25 for use in a method of treatment of ischeamia-reperfusion injury of the brain or heart, cancer, lethal hypotension in severe inflammatory conditions such as septic shock or multi-organ failure, or local and systemic inflammatory disorders including arthritis, skin disorders, inflammatory cardiac disease or migraine.

30. Use of a polynucleotide according to any one of claims 1 to 4, a polypeptide according to claim 5, an expression vector according to claim 7 or a modulator according to claim 20 or 26 for the manufacture of a medicament for use in the treatment of hyperlipidaemia, renal failure, hypertension, restenosis after angioplasty, atherosclerosis, complications of heart failure, schizophrenia, multiple sclerosis or cancer.

31. Use of a modulator according to claim 19 or 25 for the manufacture of a medicament for use in the treatment of ischeamia-reperfusion injury of the brain or heart, cancer, lethal hypotension in severe inflammatory conditions such as septic shock or

multi-organ failure, or local and systemic inflammatory disorders including arthritis, skin disorders, inflammatory cardiac disease or migraine.

32. A pharmaceutical composition comprising a polynucleotide according to any one of claims 1 to 4, a polypeptide according to claim 5, an expression vector according to claim or a modulator according to any one of claims 16 to 20 and 22 to 26 and a pharmaceutically acceptable carrier and/or diluent.

33. A method of treating a human or animal suffering from hyperlipidaemia, renal failure, hypertension, restenosis after angioplasty, atherosclerosis, complications of heart failure, schizophrenia, multiple sclerosis or cancer, which method comprises administering to the host a therapeutically effective amount of a polypeptide according to claim 5, an expression vector according to claim 7 or a modulator according to claim 20 or 26.

34. A method of treating a human or animal suffering from ischeamia-reperfusion injury of the brain or heart, cancer, lethal hypotension in severe inflammatory conditions such as septic shock or multi-organ failure, or local and systemic inflammatory disorders including arthritis, skin disorders, inflammatory cardiac disease or migraine, which method comprises administering to the host a therapeutically effective amount of a modulator according to any one of claims 19 or 25.

35. A modulator according to claim 29 for use in said method together with a methylarginine.

36. Use according to claim 31 for the manufacture of a medicament for use in said treatment together with a methylarginine.

37. A method according to claim 34, which further comprises administering to the host a methylarginine.

38. Products containing a modulator according to claim 19 or 25 and a methylarginine as a combined preparation for simultaneous, separate or sequential use in a method of treatment of ischeamia-reperfusion injury of the brain or heart, cancer, lethal hypotension in severe inflammatory conditions such as septic shock or multi-organ failure, or local and systemic inflammatory disorders including arthritis, skin disorders, inflammatory cardiac or migraine disease.

39. A modulator according to claim 35, use according to claim 36, a method

according to claim 37 or products according to claim 38, wherein the methylarginine is L-NMMA.

40. A modulator according to claim 19 or 25, which is an inhibitor of a bacterial methylarginase.

41. A modulator according to claim 40 for use in a method of treatment of the human or animal body by therapy.

42. A modulator according to claim 41 for use in the treatment of a bacterial infection.

43. Use of a modulator according to claim 40 for the manufacture of a medicament for use in the treatment of a microbial infection.

44. A pharmaceutical composition comprising a modulator according to claim 40 and a pharmaceutically acceptable carrier and/or diluent.

45. A method of treatment of a host suffering from a bacterial infection, which method comprises administering to the host a therapeutically effective amount of a modulator according to claim 40.